

REMARKS

The Office Action dated August 24, 2004 has been carefully reviewed. Claims 1, 3-5, 8-9, 11, 13, 16-26 and 33 are pending. Claims 6, 10, 12, 27 and 30 have been cancelled herein. Claims 1, 3, 4, 13, 24, and 33 have been amended. Claim 33 has been made multiply dependent upon all of the remaining independent claims of the elected Group I.

Reconsideration of the previous claim rejections is respectfully requested. Applicants thank the Examiner for her thorough and detailed remarks attached to the most recent Office Action.

Applicants believe that the amendments which have been made in response to the Examiner's most recent comments in her Rejection of the pending claims, along with the nature of this response have put the remaining claims in condition for allowance. It is therefore specifically and respectfully requested that the Examiner enter and allow the claims as amended herein.

RESPONSE TO RESTRICTION REQUIREMENT

Applicants affirm the election of Group I claims for further prosecution, and acknowledge the August 13, 2004 telephonic interview and election with the Examiner. Applicants thank the Examiner for her helpful demeanor and willingness to discuss the issues in the case during that interview. It must be noted however, that Applicants respectfully retain their rights with regard to pursuing the non-elected claims (Group II) in a separate divisional filing.

CLARIFICATION OF REJECTION TO THE CLAIMS

The Examiner is respectfully asked to clarify the rejection of claims 24 and 33.

Claim 24

In the text of the August 24, 2004 rejection, independent claim 24 is mentioned under the rejections based upon § 103(a). However, the rejections as presented do not seem to specify exactly how the prior cited art renders the full scope of the claim obvious. Clarification and a full enunciation of the rejection is respectfully again requested.

Claim 33

As amended, the multi-dependent claim 33 clearly falls within the invention of the elected claims of Group I. Reconsideration of the exclusion of this claim is requested. Should the Examiner require this claim to be cancelled since it was also dependent on a non-elected, and now cancelled, Group II claim, the Applicants will cancel, amend the text and add as a new claim. Applicants respectfully request an indication from the Examiner as to her preference.

THE REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 1-6, 8-13, 16-26 and 33 were rejected under 35 U.S.C. §112, second paragraph for being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Claims 6, 10 and 12 have been canceled herein. Each of the pending independent claims – 1, 13 and 24, has been substantially amended to address the Examiner's concerns. Applicant believes that this rejection has been thereby overcome for these claims. By amending the underlying independent claims, the dependent claims also rejected under 35 U.S.C. §112, second paragraph, are amended to comply with the Examiner's concerns for clarity of language. Reconsideration of all of the remaining pending claims is respectfully requested.

THE REJECTION UNDER 35 U.S.C. §102(b)

SU 986411

Claims 1, 3-6, 8-13 and 16-26 are rejected under 35 U.S.C. §103(a) as being unpatentable over SU 986411 [IDS – AL]. As previously noted claims 6, 10 and 12 are canceled herein.

In response to the Examiner's anticipation rejection based on the Nauk et al. citation, it should again be noted at the outset that all of the existing independent claims within this group

(claims 1, 13 and 24) have been amended to address the Examiner's concerns as to structural and grammatical problems with the claims, making it easier to compare the Nauk et al. citation and the instant invention.

Given the analysis below, the Examiner's anticipation rejections to the claims are respectfully traversed. As previously noted, the fundamental requirement necessary to maintain a rejection based on anticipation is that each and every element of the claimed invention must be disclosed in a single prior art reference or embodied in a single prior art device or practice. In re Spada, 911 F.2d 705, 15 U.S.P.Q.2d 1655 (Fed Cir. 1990); See also, Minnesota Min. & Mfg. Co. v. Johnson & Johnson Orthopedics, Inc., 976 F.2d 1559, 24 U.S.P.Q.2d (Fed Cir. 1992). That is, there must be an identity of both elements and identity of process. This SU 986411 is simply incapable of providing relevance to the amended claims of the current invention. Tyler Refrigeration v. Kysor Indus. Corp., 777 F.2d 687, 227 U.S.P.Q.177 (Fed Cir. 1986); Kalman v Kimberly-Clark Corp., 713 F.2d 760 (Fed. Cir. 1983), cert denied, 465 U.S. 1026 (1984). As was stated by the 9th Circuit:

"Unless all of the same elements are found in exactly the same situation and united in the same way to perform the identical function in prior pleaded art, there is no anticipation." Stauffer v. Slenderella Systems of California, Inc., 254 F.2d 127, 115 USPQ 347 (9th Cir. 1957).

The Examiner has stated during the prosecution of this application that with respect to the rejected claims, the SU 986411 reference is "substantially similar" or "is considered to be identical to the applicants' method for preserving mammalian sperm because they both comprise [sic] identical active steps and identical structural elements." (Office Action of August 24, 2004, p. 6 final paragraph; and see, Office Action of November 11, 2002, p. 5 final paragraph (quotation source)). Moreover, as presented above, to anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently. Inherency itself may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient; all the elements must be present. Mehl/Biophile Int'l Corp. v. Milgram, 192 F.3d 1362; 52 U.S.P.Q.2D 1303 (1999).

Therefore, in order to avoid rejection for anticipation, it is only necessary to show that independent base claims 1, 13 and 24 each contain at least one element not disclosed in SU 986411. In reviewing the teachings of the SU 986411 reference, as guided by the prior legal

precedent cited above, it is clear that the claims not only fail to recite the same elements, the actual function or "process" of utilizing the elements differs considerably. More to the point, amended claim 1 recites several elements not present or suggested in any of the teachings of SU 986411 including:

- a) stepwise mixing of said multiple cryoprotectant buffer in a manner optimized to protect the sperm cells from glycerol toxicity;
- b) Nauk et al., provides 5 temperature steps (30-15°C to 15-10°C to 10-4°C to 4-5°C to storage at -120- -140°C) while the current claims recite three different temperature steps (10-0°C to -40 – - 140°C to long term storage at -190 – 200°C). These temperature differences indicate a different appreciation for the toxicity level of glycerol and its ability to damage spermatozoa.
- c) Nauk et al., provides an explicit “glycerin equilibration” of a different temperature and length, both affecting spermatozoa toxicity differently.
- d) Nauk et al., provides for storage at a maximum of -140°C, the current claims recite a minimum long term storage temperature of -190°C. This temperature differential will effect both the duration that a sample will retain viable sperm and that motility of the sperm when eventually utilized.
- e) “wherein said second sample solution further comprises an antibiotic compound.”
Within the four corners of the current invention the “antibiotic” intended here is a substance produced by a microorganism (at least originally) that can inhibit bacterial growth and/or destroy bacteria. The Spermosan-3 composition cited by Nauk et al., apparently refers to an anti-infective compound first mentioned in the literature in 1967, and comprises a composition that is not a single compound antibiotic but has multiple anti-infective components. [No authors listed] VETERINARIJA. 1967 Apr;44(4):89. [Article in Russian]
- f) wherein said sperm sample is cooled to said first temperature and maintained at said first temperature for 4 hours to 21 hours. Not approximated by Nauk et al.

None of the elements a-f above are disclosed in the SU 986411 Nauk et al. citation. Therefore, it is respectfully proposed that the rejection of claim 1 for anticipation by the SU 986411 reference is overcome as would be any rejection based on obviousness for this citation.

Likewise, claims 13 and 24 recites several elements not present or suggested in any of the teachings of SU 986411 including:

- g) lowering the temperature of said first cryoprotectant solution to a second temperature between -60°C and -90°C wherein said first cryoprotectant solution can freeze; and
- h) wherein said first cryoprotectant solution further comprises an antibiotic compound. Please note that Spermosan-3 is not a single compound antibiotic as recited in the current claims.
- i) wherein said sperm sample is cooled to said first temperature and maintained at said first temperature for 4 hours to 21 hours.
- j) stepwise temperature protocol differences noted above.

None of the elements g-j above are disclosed in the SU 986411 reference. Therefore, it is respectfully proposed that the rejection of claims 13 and 24 for anticipation by the SU 986411 reference are again traversed.

Claims 6, 10 and 12 are canceled herein. Dependent claims 3-5, 8-9, 11, 16-23, 26 and 33 being dependent upon and further limiting independent claims 1, 13 and 24 should also be allowable for those reasons, as well as for the additional recitations they contain. Reconsideration of the rejection of the pending claims under 35 U.S.C. § 102(b), is respectfully requested.

THE REJECTION UNDER 35 U.S.C. §103(A)

SU 986411, Sikes et al., Royere et al., and Ahmad et al.

Claims 1, 3-5, 8-9, 11-13, 16-26 and 33 are rejected under 35 U.S.C. §103(a) as being unpatentable over the SU 986411 reference and the Sikes et al., (U.S. Patent No.#

3,940,943)(hereinafter the '943 patent) in view of Royere et al., and Ahmad et al. (U.S. Patent No.# 3,791,384)(hereinafter the '384 patent) The rejection of the claims, as amended, is respectfully traversed as indicated previously is traversed.

As presented in the MPEP, the basic considerations which apply to obviousness rejections are the following:

- (1) the claimed invention must be considered as a whole;
- (2) the references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;
- (3) the references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and
- (4) reasonable expectation of success is the standard by which obviousness is determined.

When the prior art itself fails to meet even one of the above criteria the cited art does not satisfy 35 U.S.C. § 103(a) and prevents the establishment of the required *prima facie* case of obviousness by the Examiner. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); In re Rijckaert, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). As pointed out below, the prior art not only fails to provide the suggestion, or incentive to combine, but also fails to provide any reasonable expectation of success for the piecemeal combination of the prior art into something resembling the instant invention.

At the outset, it should be noted that each of the remaining independent claims called out by the Examiner has again been amended to further delineate the scope of the invention, differentiate the current invention from the prior art, and to remove any ambiguities with regard to intent or grammar. With these additional changes the Applicants believe that the claims are in no way obvious in light pursuant to the cited prior art. That is, the limitations of the cited prior art, in particular SU 986411 as cited here and with reference to discussion of any possibility of the Nauk et al. citation forming the basis of an anticipation or obviousness rejection. Moreover, the '943 patent and Royere et al., have each been reviewed and the claims as amended include limitations not taught by any of this prior art alone or in combination. (Please see pages 8 and 9 of the Rejection of August 24, 2004).

SU 986411

As stated in the last action, the SU 986411 provides some insight into the use of a cryoprotectant buffer and methodology somewhat similar in objective to the current invention, but importantly they differ in the stepwise methodology used in accomplishing this objective as noted above. For example, the concentrations of cryoprotectant components other than glycerol differ in amount and in concentration (e.g., fructose, citric acid, Tris, optimal concentration of egg yolk or the presence of antibiotics). This basic difference in functional cryoprotectant solutions, was respectfully, not addressed by the Examiner. These changes in cryoprotectant composition and in the stepwise development of that composition lead inexorably to a new buffer with different characteristics and advantages and a completely different character. The SU 986411 reference provides: 1) no optimized concentrations or amounts of what compounds to be added to the composition whatsoever; 2) no protocols for mixture other than a 5 step temperature protocol, and 3) fails to provide any guidance for the stepwise cooling protocol of the current invention. This lack of guidance, lack of anything resembling “teaching” the invention is clear. Given this, and the controlling precedent cited the SU 986411 reference simply cannot render obvious any of the current independent claims, or those claims that in turn are dependent upon them. These deficiencies are not fully remedied through the use of the other citations provided by the Examiner. That is, though the SU 986411 reference and other citations are tasked to providing a solution to the same or similar problem as that faced by the Applicants, the cited prior art and the Applicant simply found different methods to solve the problem.

Sikes et al.

Sikes et al., ('943 patent) simply does not provide what SU 986411 lacks. Respectfully, and as already stated, Sikes presents the state of the art as of 1975, and does not teach the invention as presented by Applicants. That is, it does not present a cryoprotectant buffer similar to the one employed by the Applicants as found in the amended independent claims. Nor can it teach any combination with SU 986411.

The '943 patent states to add the cryoprotectant glycerol immediately after collection of a sperm sample. According to the current invention any glycerol use is added to the sperm sample only if it has collected and cooled for 4 to 21 hours. The importance of this is to avoid glycerol toxicity. This is one of the fundamental utilities of the current invention. One measure of the

novelty of the current claims is the fact that they overcome the limitations of the past in terms of prior art inefficiencies, such as glycerol toxicity as related to spermatozoa utility and motility when thawed for use. The '943 patent cannot sustain an obviousness rejection alone or in combination due to the many deficiencies in its teachings. Some of these, vis-à-vis the amended independent claims provide:

- a) wherein said sperm sample is cooled to said first temperature and maintained at said first temperature for 4 hours to 21 hours;
- b) wherein said first cryoprotectant solution further comprises an antibiotic compound.
- c) the presence of a tris buffer.
- d) the presence of citric acid.
- e) any egg yolk concentration.
- f) any fructose use or concentration.

This laundry list of deficiencies serves to, respectfully, point out why Sikes is simply inapposite to the current claims and cannot sustain an obviousness rejection. (Please see pages 8 and 9 of the Rejection of August 24, 2004).

Thus, amended independent claims 1, 13 and 24 cannot be obvious over Sikes et al., either alone or in combination with SU 986411 given these remarks and those already provided under the Examiner's anticipation rejections. Likewise, those claims dependent upon these independent claims are not obvious due to the above remarks and their own additional limitations.

Royere et al.

Respectfully, it must be reiterated that the Examiner's use of Royere et al. is useful only to point out the weakness of the prior art and the failure of the cited prior art to function together in combination to render the instant claims obvious. Moreover, this citation also simply fails to provide what the Nauk et al. SU 986411 citation and Sikes et al., citations lack.

Royere et al., is a review article of the changes in the sperm preservation art over the last several decades. In this sense it catalogs what has gone before and in fact teaches against the methods of both Sikes and SU 986411, describing them as the “old methods” and not “truly rational” (please see, Royere et al., Conclusions p. 557 relevant to anything more than 10 years old in the field, that is, available prior to 1985)(SU 986411 published 1979, and Sikes et al., issued 1975), preventing any combination. Thus, Royere not only teaches away from SU 986411 and Sikes, its teachings prevent any combination from being made, and its own limitations help to underscore the patentability of the current invention. Specifically:

- 1) No mention is made of the cryoprotectant composition provided by the current invention,
- 2) No stepwise cooling system as provided by the claims is presented,
- 3) No selection of antibiotics or concentration of egg yolk is taught.

Rather, Royere et al., simply reviews the field and points out prior deficiencies. The present invention, as recited in amended independent claims 1, 13, and 24 offers the benefits of a novel structural methods and a different cryoprotectant composition. If the invention as recited were obvious, then those skilled in the art would have long since adopted this invention. However, according to the art of record, those skilled in the art have not adopted the present invention, and therefore do not get the benefit of the invention. (Please see pages 8 and 9 of the Final Rejection of August 24, 2004).

It is important to reiterate that the standard for sustaining an obviousness rejection is not whether the methods used in comparison to those disclosed in a given invention are appropriate or mimic the disclosure, but whether there is some quantifiable reason in the cited references or art available generally to the artisan in the field to combine the works to defeat patentability. Indeed, to combine multiple references in an effort to defeat patentability without some objective indicator within the art that such a combination would be appropriate is a classic representation of improper hindsight. In re Dillon, 919 F.2d at 696, 16 USPQ2d at 1904 (Fed. Cir. 1990)(*en banc*); In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). The art presented by the Examiner simply does not accomplish this task, not only because it art cannot be combined, but also

because the citations relied upon by the Examiner teach away from the subject matter of the claims, whether taken together or separately.

Given the above, it is proposed that independent claims 1, 13 and 24 and those claims in turn dependent upon them, cannot be obvious.

The dependent claims being dependent upon and further limiting independent amended claims 1, 13, and 24, should also be allowable for that reason, as well as for the additional recitations they contain. Applicants respectfully request reconsideration of the rejection of the claims under 35 U.S.C. § 103(a) in view of the above amendments and remarks.

Amended multiple dependent claim 33 has similar limitations to those discussed above, including claim 13 or as the case may be. As it retains all the elements of the amended base claims from which it depends it should be allowable for this reason, as well as for the additional recitations it contains. Applicants therefore respectfully request favorable consideration of the claims under 35 U.S.C. § 103(a), in view of the above amendments and remarks.

Ahmad et al.

The Ahmad et al., reference does not provide what the above citations lack (United States Patent 3,791,384). As stated by the Examiner, this citation is provided to “demonstrate the use of antibiotics...in the solutions in the methods for preserving mammalian sperm.” (Rejection of August 24, 2004, page 10). However, before Ahmad can be of use in the list of cited prior art, the Examiner must show that the cited artisans showed some indication that the specific features of prior inventions or modifications could or should be combined to better effect. That is, if art is to be combined, the cited **art must at least** indicate that a combination would be possible and desirable in order to render a future combination of that art obvious to one skilled in the relevant field. Ahmad does not do this.

Richter et al.

U.S. Pat. No. 3,791,384 (to Richter et al.) discloses a method for deep freezing and thawing boar sperm which includes inactivating the fresh sperm by means of an inactivating solution that includes dextrose, a dihydrate of EDTA, sodium citrate and sodium hydrogencarbonate. The Richter et al., solution comprises an aqueous suspending vehicle which

is physiologically acceptable to the cells and which contains this alternate solution – not present, claimed or desirable for the current invention. More to the point, Richter et al., neither cites nor uses glycerol and reports that the cryoprotectant solution of the reference provides an ability to resist freezing.

For the reasons given above and the fact that the Royere et al., Sikes et al, Richter et al., and SU 986411 references each fail to do this has been made clear. Therefore, no combination is possible. More to the point, the fact that all of the prior art is insufficient to foster the combination means that either Richter and/or Ahmad must do this. This being the case, the Ahmad et al., reference itself must then present or imply all the features rejected by the Examiner within its four corners. However, the fact is that the rejected features were not so suggested or inferentially implied by this citation, and that, therefore no rejection on the basis of obviousness can be maintained. In re Dillon, 919 F.2d at 696, 16 USPQ2d at 1904 (Fed. Cir. 1990)(*en banc*); In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Likewise, Richter is ostensibly cited only because it employs streptomycin, Tris, fructose and citric acid. (Richter Columns 3-5).

The differences between the claimed methods and the Ahmad citation are, as laid out above, substantial and include *several* reasons why no rejections based on this prior art reference render the application obvious or anticipated. With respect to one particular element, Applicant points to the use of tris and/or citric acid in the cryoprotectant buffer. As previously stated, *the prima facie* case that the Examiner must provide is one of factual, objective evidence. Otherwise the combination cobbled together is a species of simply improper hindsight and speculation. Dillon; *and see*, In re Chevenard, 139 F.2d 71, 60 USPQ 239 (CCPA 1943)(Appellant reserves the right to challenge any objective evidence presented by the Examiner); 37 CFR § 1.107. Barring such an affirmative assertion the analysis already provided is sufficient to defeat any obviousness rejection.

COMPLIANCE WITH 37 CFR § 1.111(B)-(C)

Subsection B

Applicants respectfully request clarification relative to the Examiners rejection under 37 CFR § 1.111(b) as it appears to be a new ground of rejection that has not been put forward before, and relates to the fundamental structure of the claims and specification as well as the Applicants repeated *bona fide* responses in this case – both before and after the Request for Continued Examination. Alternatively, if it is an additional expression as to the Examiner's belief that there is no patentable claims to be found in the Applicants efforts then its place is likely to be more appropriate as part of an obviousness rejection or anticipation rejection on the basis of cited prior art. In response to these prior art citations the specific distinctions between the current claims have been laid out several times by Applicants, as well as claim amendments being made or claims actually being cancelled in attempt to generate allowable subject matter over the prior art.

Respectfully, the *prima facie* case that the Examiner must provide is one of factual, objective evidence. If the Examiner seeks to introduce as fact a personal opinion, the appropriate means is through the completion of an affidavit or declaration; short of this, speculative comments or bare assertions are improper. In re Pardo, 214 USPQ 673, 677 (CCPA 1982); In re Chevenard, 139 F.2d 71, 60 USPQ 239 (C.C.P.A. 1943) (Applicant also respectfully reserves the right to challenge any objective evidence presented by the Examiner); 37 CFR § 1.107. Barring such an affirmative assertion the analysis already provided is sufficient to defeat any objection based on 37 CFR § 1.111(b)-(c).

Moreover, as is indicated by the citation of this rule, the Examiner appears to be stating as a grounds of rejection that the Inventors have not distinctly and specifically pointed out the supposed errors in the Examiner's "*prima facie*" case of obviousness or anticipation and/or replied to every ground of objection and rejection in the prior Office action(s). That is, it is incumbent upon the Applicants to insure that each reply must present arguments pointing out the specific distinctions believed to render the claims, including any newly presented claims, patentable over any of the applied prior art references. If this is the substance of the rejection then Applicants point to the prosecution history of this case in which they believe that they have, respectfully, repeatedly pointed out the distinctions between the current claims and the prior art. Applicants also point out to the responses to the statutory rejections also provided in this latest Amendment. These *bona fide*

attempts to overcome the cited prior art obviate any objections or rejections over 37 CFR § 1.111(b) or (c). Thus, Applicants respectfully traverse this objection.

If this is insufficient to overcome the hurdle of 37 CFR 1.111(b) they also point to the specification itself which provides in relevant part:

“The production of founder transgenic animals, however, can be expensive. Male animals with valuable genetics are often lost unexpectedly. These unexpected deaths can present the owner with a great financial loss, and more importantly the loss of the animal’s genetics if offspring were not produced or semen cryopreserved. In a transgenic production setting, the loss of a founder male has a significant economic impact and disrupts the time frame for projects.

The genetic material from many species has been preserved and passed on by using artificial insemination and in vitro fertilization techniques. The process of freezing spermatozoa can be harsh as a result of thermal, osmotic, and/or mechanical shock to the cell, and the formation of crystals, which can damage cellular structures, particularly the plasma membrane. In addition, the process of freezing and thawing causes dehydration of the cell with potential for cellular damage. Methods that overcome these obstacles are useful for preserving sperm for any number of purposes, e.g., medical, commercial, and agricultural purposes.” (Specification, “Background of the Invention” for the current filing).

The above must be viewed with the understanding that the current filing was done to overcome the shortcomings of the described prior art difficulties. Again, Applicants respectfully traverse this rejection. Reconsideration is requested.

Subsection C

Applicants also respectfully request clarification relative to the Examiners rejection under 37 CFR § 1.111(c) as it also appears to be a new ground of rejection that has not been forwarded before, and again relates to the fundamental structure of the claims and amendments thereto.

That is, an Applicant’s reply must appear throughout to be a bona fide attempt to advance the application or the reexamination proceeding to final action. Applicants categorically state that this has been their intention throughout prosecution on this case. Moreover, Applicants point to the above remarks and the repeated *bona fide* responses in this case – both before and after the Request for Continued Examination, as well as the amendments contained herein.

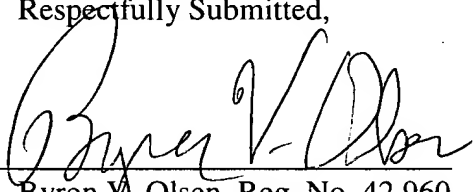
Reconsideration is requested.

The Commissioner is authorized to charge any fee which may now or hereafter be due for this application to GTC Biotherapeutics' Deposit Account No. 502092.

Applicants respectfully submit that the pending claims of this application are in condition for allowance, and that this case is now in condition for allowance of all claims therein. Such action is thus respectfully requested. If the Examiner disagrees, or believes for any other reason that direct contact with Applicant's attorney would advance the generation of any allowable subject matter, the Examiner is invited to telephone the undersigned at the number given below.

Early and favorable action is earnestly solicited.

Date: 2/23/05

Respectfully Submitted,

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